



Phase I Clinical Trials



Department of Investigational Cancer Therapeutics

THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

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FDA Grants Expanded Access to Unapproved Investigational Drugs Outside of a Clinical Trial



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Nearly three years after the FDA put forth a proposal to expand access to investigational new drugs for patients with serious or life-threatening conditions who lack other treatment options, new expanded access regulations went into effect in October 2009. [For an in-depth discussion of improving access to investigational drugs, see the Winter/Spring 2007 issue of this

newsletter.] Unlike the intent of the traditional investigational new drug IND, which focuses on safety and effectiveness, the intent of the new expanded access rule's IND application is treatment using an unapproved drug outside of a clinical trial.

The use can be for individual access by one patient or intermediate-size population use by an estimated ten to 100 patients. Populations substantially larger than this are expected to be transitioned to a treatment protocol or IND as soon as there is sufficient evidence to support it. The applicant must convince the FDA that the potential benefit to the patient justifies the potential risk of using the treatment. Evidentiary standards needed for access decrease as the seriousness of the condition increases and the size of the population to be treated decreases. This new FDA final rule allows access to these investigational drugs only if it will not interfere with clinical investigations leading to the marketing approval and widespread availability of the drug.

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**FROM
THE
CHAIR**

Patients with PIK3CA Mutations in Advanced Cancers Respond to PI3K/AKT/mTOR Pathway Inhibitors



Filip Janku, MD, PhD, landed at M. D. Anderson by way of the Czech Republic and Ireland, where he had already completed training in medical oncology, to investigate the phosphatidylinositol-3-kinase (PI3K)/AKT/mTOR pathway as a clinical research fellow in the Department of Investigational Cancer Therapeutics (ICT). Dr. Janku, under the mentorship of Razelle Kurzrock, MD, chair of the department, has studied the results of treating patients with agents that specifically target this pathway. He notes that this pathway is particularly important in cancer because it is overactive in many tumors, appears to drive carcinogenesis, and can be targeted for prevention and therapy. Dr. Janku has analyzed the results of a group of studies in which patients with mutations in the *PIK3CA* subunit of PI3K, along with co-existing mutations that may confer resistance to PI3K inhibition, are enrolled on trials that affect this abnormal signal. "This is a mutation we can actually look at," he said, "And some drugs targeting the pathway such as mTOR inhibitors are already commercially available." Thirteen single drug or combination trials that include a PI3K pathway inhibitor (most targeting mTOR, two PI3K) are available in ICT, and an additional combination trial is in the works.

The results of this research demonstrated that *PIK3CA* mutations were present in 11.5% of 217 patient samples. These mutations were found most frequently in endometrial, ovarian, colorectal, breast, cervical, lung, and head and neck cancers. The 17 patients with mutations who were treated with a drug that targeted this signaling pathway showed a response rate of 35%. While the number of patients is still small, this response rate is considerably higher than the 4 to 11% response rate generally seen in phase I trials, when patients are treated in an unselected fashion. An additional finding accounted for some of the non-responders. No patients with colorectal cancer who had a co-existing *K-RAS* mutation responded to PI3K pathway inhibitors. However, even though *RAS* or *RAF* mutations are believed to confer resistance based on animal data, patients with ovarian cancer who had additional *K-RAS* or *B-RAF* mutations were not resistant to therapy. Some of the results from 117 of these samples were recently highlighted at the American Association for Cancer Research (AACR) International Conference on Molecular Targets and Cancer Therapeutics held in November 2009.

"This work is an example of how we can optimize cancer therapy through personalized treatment. We now are in a unique position to move the field forward. The fruit of three or more decades of basic research can now be harvested in the clinic," Dr. Kurzrock remarked. "Numerous targeted agents are in clinical trials. These drugs preferentially impact the cancer cell, so remarkable responses can be seen, often with minimal to no side effects. But you have to give the right drug to the right patient. Even insulin is a poor drug if you give it to a patient with pneumonia; you have to give it to a diabetic. For the first time, we have the technology to test a patient's molecular profile and match the patient with the right drug. We can't do that for everyone yet, but our Pathology department is doing a wonderful job of getting these tests in place, and our department and others at MD Anderson Cancer Center are moving quickly toward that goal."

Why M. D. Anderson?

- We are ranked #1 nationwide in cancer care by *U.S. News & World Report*.
- We lead the way nationally in National Cancer Institute grant awards dollars, receiving nearly \$200 million annually.
- We have 13 specialized Programs of Research Excellence (SPORE) awards from the National Institutes of Health, more than any other institution in the country.
- We see 96,500 cancer patients per year, 33,200 of them new patients.
- Nearly 12,000 patients are on therapeutic clinical trials.

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Courage and Dual Death Receptor Defeat Chondrosarcoma

In the Summer/Fall 2006 issue of this newsletter, we mentioned a patient with chondrosarcoma with lung metastases who'd had a dramatic partial response to recombinant human Apo2L/TRAIL, a tumor necrosis-related ligand that induces apoptosis by directly activating the pro-apoptotic death receptors DR4 and DR5, even in the absence of the p53 tumor suppressor gene. That patient was Joel Kilpatrick, a former restaurant manager in Houston, and we are jubilant that 78 drug cycles and 55 months after starting on this therapy, he continues to thrive at age 63.

Mr. Kilpatrick was no stranger to cancer when he was referred to MD Anderson in 1995 with a synovial chondroma of the left elbow, which proved to be chondrosarcoma, a spindle cell neoplasm of bone typically occurring in middle age. A former smoker who had quit in 1988, he had already survived a grade 1 papillary cell carcinoma of the bladder in 1990 and then parathyroid cancer in 2000. He'd also had several previous surgeries for problems with his left elbow

while in his mid 20's. After a left elbow fusion in 1995 failed to prevent disease recurrence, he had an above-elbow amputation when the disease recurred as a grade 3 chondrosarcoma. "Mr. Kilpatrick has endured many challenges," Renee Thompson, research data coordinator, remarked. "We appreciate his courage."

"Losing my arm was very hard for me to deal with," said Kilpatrick, as he told his story at a Department of Investigational Cancer Therapeutics staff meeting on March 8, 2010. "I was concerned about my appearance, how other people would look at me and deal with me. But the worst problem I've had to deal with was phantom pain. I was unprepared for the unrelenting pain, and I had to quit my job." The chondrosarcoma returned in 1998, and Kilpatrick had to have a second amputation—this time a shoulder disarticulation, which he said further increased his phantom pain. "I had more problems with my self-image, and began to have fears about my mortality." In 2000, he had a left axillary recurrence indicating metastatic chondrosarcoma, which was treated with radiation. "Then I became despondent," he added, "I had to get over the fatigue. I had to find the energy to get back on my feet, to get out of bed for a day."

By 2003, Kilpatrick had bilateral lung metastases, which was treated with six cycles of irinotecan. "I had so many side effects on this treatment that it was hard to tell if the cancer or the treatment was worse," he noted. The irinotecan-based regimen left him with stable disease, but he had progressive disease within eight months, and in 2004, had a wide excision of the left anterior chest wall.

Unfortunately, Kilpatrick's disease continued to progress, and, having exhausted all standard treatment options, he was referred to the Phase I Program in 2005, where he started on rhApo2L/TRAIL therapy on August 1, 2005. Roy Herbst, MD, PhD, a professor in the Department of Thoracic/Head and Neck Medical Oncology, was principal investigator of this study, and Terri Warren, RN, MSN, was the research nurse supervisor. Kilpatrick was pleasantly surprised, especially after his many previous experiences with cancer treatment, to find that he had no side effects on the TRAIL therapy. Asked how he felt about going on a first-in-humans drug, Kilpatrick replied, "It was a little scary, but I felt that given my cancer, it seemed the right choice." Given his excellent and long-lasting response, it appears that Apo2L/TRAIL therapy was indeed the right choice for Joel Kilpatrick.

UNAPPROVED INVESTIGATIONAL DRUGS *continued from page 1*

How to Apply

The drug developer or any licensed physician can submit an IND application to obtain permission from the FDA to administer an investigational drug to an individual patient or group of patients outside of a clinical trial. Most of the data required can come from reference to the content of an IND held by the pharmaceutical company or other sponsor who is developing the drug for marketing. As explained in the *Federal Register*, August 13, 2009, the physician need only add information that is typically recorded during routine patient care.

The applicant must describe:

- Rationale for the intended use;
- Why there are no comparable or satisfactory therapeutic alternatives;
- Criteria for patient selection, or description of the individual patient's disease, including recent medical history and previous treatments;
- Method of administration, dose, and duration of therapy;
- Description of the facility where the drug will be manufactured;
- Pharmacology and toxicology information demonstrating drug is reasonably safe;
- Monitoring, testing, or other procedures needed to evaluate the effect of the drug and to minimize risks to the patient.

The intent of the expanded access for an intermediate-size patient population IND is to make a drug under development available to patients who cannot enroll in a clinical trial, or to make a drug available that does not have an adequate size market to develop. The FDA feels this will not interfere with the drug's development and progression to market because the drug sponsor is unlikely to provide expanded access in cases where drug development would be impeded, as it is not in their best interest to delay commercial sale of a drug.

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OPPORTUNITIES FOR

Training in Clinical Trials Research Offered

Physicians seeking advanced training in clinical and translational research may benefit from enrollment in two programs directed by Razelle Kurzrock, MD, chair of the Department of Investigational Therapeutics: The Phase I Clinical Trials Fellowship Program and the MS/PhD Program in Patient-Based Biological Research as part of The University of Texas Graduate Studies in Biomedical Sciences (GSBS) program.

Founded in 2005, the clinical trials fellowship program supports six fellows annually, providing one year of training in clinical trials research, with the option to extend it for a second year to complete a project. "The interest in the clinical trials fellowship began in Internal Medicine, but physicians from multiple subspecialties could benefit from this training," said Dr. Kurzrock. "For example, we've had two fellows come from a gynecologic surgery background."

While most fellows begin in July, they can also begin off cycle, noted Denise de la Cruz Baum, MEd, ICT manager of clinical protocol administration. She also serves as a liaison between the fellows and the Trainee and Alumni Affairs Office, which recruits the fellows. "I take care of any issues that may arise such as appointments, interviews, and the application process," said Baum.

Fellows have the opportunity to pursue their own research interests, and must develop a study protocol during their first year. "We offer a wealth of opportunity for interaction with a wide variety of investigators who have internationally acclaimed expertise in basic, translational, and clinical science," said Dr. Kurzrock. Fellows in the program will gain experience in writing trial protocols, interacting with drug sponsors, developing translational endpoints to understand a drug's impact and factors predicting a patient's response to a drug and its toxicity, presenting data at national and international meetings, analyzing data, and writing scientific articles for publication.

Fellows also get hands-on experience caring for patients who have a variety of advanced cancers. They spend two months on the inpatient service and three days a week in the outpatient Clinical Center for Targeted Therapy. They are also required to attend the weekly ICT staff meeting and the weekly phase I treatment planning meeting.

Physicians who have a strong interest in a career in oncology drug development, and who have completed their internal medicine residency or equivalent training, should contact Dr. Kurzrock or Denise Baum, then apply to the clinical trials fellowship program through the Trainee and Alumni Affairs Office, which posts application materials and instructions on their web site. Completion of medical oncology training is preferred but not required. Physicians enrolled in this fellowship program may also obtain an MS or PhD in Human Biology and Patient-Based Research through The University of Texas Graduate School of Biomedical Sciences (GSBS) or audit courses in that program.

Anyone interested in applying to these programs should contact Denise Baum, MEd, manager of clinical protocol administration, email: ddbaum@mdanderson.org.

GSBS Training in Patient-Based Biological Research

The MS/PhD Program in Patient-Based Biological Research should especially appeal to basic laboratory scientists preparing for careers in translational research and physicians who wish to apply scientific knowledge and rigorous research methodology to patient-based investigation. Students must apply to GSBS for an MS or PhD in order to add on the course requirements for specialized training in patient-based biological research. However, anyone at MD Anderson can audit six credits for free as a non-degree-seeking student, said Baum.

Courses offered include:

- Human Protocol Research
- Translational Sciences: Bench to Bedside and Back
- Seminars in Clinical Cancer Research
- Seminars in Clinical Cancer Treatment
- Biomedical Statistics
- Grant and Manuscript Writing
- Ethics in Clinical Trials Research

The students also had the opportunity to evaluate their courses and identify other beneficial topics. "They particularly valued the ethics class, which was offered for the first time this semester," Baum remarked.

Winter Summit

Held annually, the Winter Summit has a dual purpose: to give students and trainees the opportunity to present their research findings and to get to know the other students and their mentors, said Baum. This year's summit was held in February and organized by Dr. Khandan Keyomarsi, professor in Radiation Oncology at MD Anderson and a member of the GSBS. Attendees included clinical and translational science researchers, and T32 training grant recipients, K12 scholars, CTSA trainees and their mentors, MD/PhD students, and Triumph fellows, a fellowship program also directed by Dr. Keyomarsi.



Back row, L-R, current clinical research fellows: Jesal Patel, MD; Ernesto Bustinza-Linares, MD; Christos Vakilavas, MD; Ignacio Garrido-Laguna, MD; Hazem El Osta, MD; Filip Janku, MD (not pictured). **Middle row, L-R,** faculty: Jennifer Wheler, MD; Aung Naing, MD; Gerald Falchook, MD; David Hong, MD; Sarina Piha-Paul, MD. **Seated, L-R,** Siqing Fu, MD, PhD; Razelle Kurzrock, MD, chair; Apostolia Tsimberidou, MD, PhD

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Did You Know That in Fiscal Year 2009...

- There were 102 phase I clinical trials on the program's priority list?
- 820 patients were enrolled in phase I trials?
- The Clinical Center for Targeted Therapy had 8,686 patient visits—2,668 more than in 2008?
- The department received more than \$12.6 million in peer-reviewed and sponsored research?
- This became the largest program in the world expediting the development of early phase clinical trials of new cancer therapeutic agents?

The goals for phase I trials in the next couple years are to:

- Move the program toward personalized therapy, fingerprinting patients to predict potential response, and identify preliminary subsets of responsive patients to use as a foundation for phase II studies.
- Enhance the capacity of phase I studies to serve as a conduit to phase II efficacy studies, especially for uncommon tumors, so that early evidence of response can be quickly translated into new treatment.
- Have a large number of high-impact studies, aiming to investigate "the best molecules in the nation."
- Emphasize strongly the quality of patient care, keeping in mind that the patient must always come first, not the study.
- Continue to foster team work and a collaborative atmosphere both within the program and in its interactions with other investigators throughout the institution, so that the ultimate goal of bringing new therapies to cancer patients can be met.
- Further develop the phase I infrastructure, from faculty to research nurses, coordinators and other personnel, in order to maximize program growth and excellence.

UNAPPROVED INVESTIGATIONAL DRUGS *continued from page 2*

Obstacles to Providing Real Expanded Access and Guidelines to Charging for Investigational Drugs

"Drug sponsors may not have any incentive to participate in expanded access to experimental drugs, and the FDA can't compel companies to provide the drug," said Christos Vaklavas, MD, a clinical research fellow in the Department of Investigational Cancer Therapeutics, in discussing hurdles to providing expanded access. He also views covering the cost of the drugs to be a "big black box." In an attempt to eliminate financial disincentives to industry providing unapproved drugs outside of clinical trials, the FDA is allowing companies to recover the direct costs of manufacturing the drug specific to the expanded treatment access, but they must first apply to obtain authorization from the FDA, supplying written support justifying the specific charges. When use is expanded for intermediate-size patient populations and treatment INDs, the sponsor may charge for the cost of administering the program as well as the direct costs of making the drug. Charging must not interfere with development of the drug for marketing approval. Recognizing that the inability of patients to pay out-of-pocket costs could limit access to investigational drugs, the FDA encourages insurance companies to reimburse care associated with administration of the drugs as they would care in a clinical trial. But the FDA is not authorized to force insurance companies to cover these drugs.

After Expanded Access Approval

Treatment on an expanded access basis may begin 30 days after the FDA receives the IND or earlier if FDA notification has been received. Retrospective institutional IRB approval is required. In a true emergency when the patient must be treated before a written submission and approval can be made, the FDA may authorize use of a drug by phone. After treatment, the physician is required to submit a written summary of the results of using the investigational drug under the expanded access regulations, including any adverse effects.

Emil Freireich, MD, professor in Leukemia, lamenting that there have been too many instances where good drugs were destroyed by the regulatory process, would like to see regulation of untested drugs move from the FDA to the cancer centers, "where the true expertise is." He noted that in Great Britain, £400,000 goes to cancer centers annually for drug regulation. "There is a precedent," said Dr. Freireich, "So why can't we do this in the United States?"

The FDA's Office of Special Health Issues will assist physicians in complying with expanded access regulations: <http://www.fda.gov/oashi/home.html>.



Active PHASE I PROGRAM PROTOCOLS

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
*PXD101	George Blumenschein, Jr., MD	Histone deacetylase inhibitor	Solid tumors	
*SU011248 and paclitaxel/carboplatin	George Blumenschein, Jr., MD	Multi-kinase inhibition of VEGF, PDGF, CKIT, FLT-3	Solid tumors	Allows CNS metastases
BAY 73-4506	George Blumenschein, Jr., MD	Multi-kinase (raf, VEGFR, PDGFR) inhibitor	Advanced cancers	
Azacytidine and valproic acid + carboplatin	Gerald Falchook, MD	Histone deacetylase inhibitor, hypomethylating agent, and chemotherapeutic agent	Ovarian cancer	
Bevacizumab and bortezomib	Gerald Falchook, MD	Anti-angiogenic agent and proteasome inhibitor	Advanced cancers	Allows children any age and CNS metastases
Bevacizumab and 1) sunitinib 2) sorafenib 3) erlotinib and cituximab 4) trastuzumab and lapatinib	Gerald Falchook, MD	Anti-angiogenic agent and MKI, EGFR inhibitor, HER2 inhibitor	Advanced cancers	Allows children any age and CNS metastases
GSK 2118436	Gerald Falchook, MD	BRAF inhibitor	Solid tumors	
MLN8237	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
MLN8237 (enteric coated tablet)	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
EMD1214063	Gerald Falchook, MD	cMET inhibitor	Advanced cancer	Allows CNS metastases
GSK 1120212	Gerald Falchook, MD	MEK inhibitor	Advanced cancer	Allows CNS metastases
*ABI-009	Ana Gonzalez-Angulo, MD	Albumin-tagged mTOR inhibitor	Solid tumors	
*AMG655	Roy Herbst, MD, PhD	Activating peptide against death receptor (DR5)	Advanced cancers	No CNS metastases
*AG-013736 and paclitaxel/carboplatin; AG-013736 and docetaxel/carboplatin	Roy Herbst, MD, PhD	Anti-angiogenesis with chemotherapy	Solid tumors	Allows CNS metastases
*BMS-690514	Roy Herbst, MD, PhD	Pan-HER/VEGFR-2 tyrosine kinase inhibitor	Solid tumors	
PX-478	Roy Herbst, MD, PhD	HIF-1alpha inhibitor	Advanced cancers	Allows CNS metastases
PX866	Roy Herbst, MD	PI3K inhibitor	Solid tumors	
*PRO 1762 (TRAIL)	Roy Herbst, MD	Tumor necrosis-related, apoptosis-inducing ligand	Solid tumors, non-Hodgkins lymphoma	
AMG 386 with: 1) AMG 706 2) bevacizumab; or 3) sorafenib	David S. Hong, MD	Combines 2 anti-angiogenic agents	Solid tumors	Allows CNS metastases
*Tipifarnib and sorafenib	David Hong, MD	Combines farnesyltransferase inhibitor (tipifarnib) with raf kinase/ VEGFR inhibitor (sorafenib)	Advanced cancers	
E7080	David Hong, MD	Angiogenesis inhibitor	Advanced cancers	
*Gemcitabine and dasatinib	David Hong, MD	Src inhibitor and anti-metabolite	Solid tumors	Allows CNS metastases
AZD2171 and bevacizumab	David Hong, MD	VEGF Inhibitor	Advanced cancers	Allows CNS metastases
*E7107	David Hong, MD	VEGFR Inhibitor	Solid tumors	
PBI-05204	David Hong, M. D.	Cytotoxic agent	Advanced cancers	
*LY2275796	David Hong, MD	Antisense, inhibits eukaryotic initiation factor	Advanced cancers	Allows CNS metastases
BIIB028	David Hong, MD	Hsp90 inhibitor	Solid tumors	
AMG 208	David Hong, MD	c-MET inhibitor	Solid tumors	
MABp1	David Hong, MD	IL-1a inhibitor (human monoclonal antibody)	Advanced cancers	Allows CNS metastases
*RO4858696	Razelle Kurzrock, MD	Monoclonal antibody against IGF-1R	Advanced cancers	Allows CNS metastases
Olanzapine	Razelle Kurzrock, MD	Atypical neuroleptic	Advanced cancers with cachexia	
R7112	Razelle Kurzrock, MD	MDM2 antagonist	Advanced cancer	
NPI-0052	Razelle Kurzrock, MD	Proteasome inhibitor	Advanced cancers	No CNS metastases
*Amplimexon and taxotere	Razelle Kurzrock, MD	Depletes glutathione, iminopyrrolidone with chemotherapy	Non-small cell lung, breast, prostate cancers	Allows CNS metastases
XL-184	Razelle Kurzrock, MD	Met kinase and VEGFR inhibitor	Advanced cancers	No CNS metastases
Doxil, gemcitabine, and velcade	Razelle Kurzrock, MD	Chemotherapy with proteasome inhibitor	Advanced cancers	Allows children any age and CNS metastases
CNTO 328	Razelle Kurzrock, MD	Antibody against interleukin-6	Castleman's disease, lymphoid tumors, myeloma	No CNS metastases
*Neumega	Razelle Kurzrock, MD	Interleukin-11, hematopoietic growth factor	Myelodysplastic syndrome	Phase II
Curcumin	Razelle Kurzrock, MD	Plant-derived NFκB inhibitor	Pancreatic cancer	Phase II
*XL-844	Razelle Kurzrock, MD	Kinase inhibitor and cytotoxic agent	Advanced cancers	
AZD8330	Razelle Kurzrock, MD	MEK inhibitor	Advanced cancers	Allows CNS metastases
*ANG1005	Razelle Kurzrock, MD	Mitotic inhibitor combined with amino acid peptide (crosses blood-brain barrier)	Solid tumors	
Hepatic arterial infusion with abraxane	Razelle Kurzrock, MD	Anti-microtubule agent	Solid tumors	
Doxil, bevacizumab, temsirolimus	Razelle Kurzrock, MD	Anthracycline antibiotic, monoclonal antibody, and mTOR inhibitor	Advanced cancer	Allows children and CNS metastases
Temsirolimus, topotecan, and bortezomib	Razelle Kurzrock, MD	mTOR inhibitor, combined with topoisomerase and proteasome inhibitors	Advanced cancer	Allows children and CNS metastases
R1507 12 arm study	Razelle Kurzrock, MD	IGF-1R antagonist and multiple standard chemotherapies	Advanced cancers and primary brain tumor	Allows CNS metastases
CNTO328	Razelle Kurzrock, MD	IL-6 monoclonal antibody	Solid tumors	
Torisel and PI3 kinase mutations	Razelle Kurzrock, MD	mTOR inhibitor	Advanced cancer	
OPB-31121	Razelle Kurzrock, MD	STAT3 inhibitor	Solid tumors	
Sirolimus and cetuximab	Razelle Kurzrock, MD	mTOR inhibitor, anti-EGFR monoclonal antibody	Advanced cancer	Allows children and CNS metastases
XL-184 randomized discontinuation	Razelle Kurzrock, MD	MET/RET/VEGFR kinase inhibitor	Advanced cancer	
GSK 2126458	Razelle Kurzrock, MD	PI3K inhibitor	Advanced cancer	Allows CNS metastases
Dasatinib, bevacizumab, paclitaxel	Razelle Kurzrock, MD	Src inhibitor combined with anti-VEGF monoclonal antibody and microtubule inhibitor	Advanced cancer	Liver predominant disease. Allows children any age and CNS metastases
Docetaxel and sirolimus	Razelle Kurzrock, MD	mTOR inhibitor and antimitotic agent	Advanced cancer	Allows children any age and CNS metastases

* Closed to new patient entry

Continued on reverse side

TREATMENT PLANNING CONFERENCE

Referring physicians and nurses who want to present patients for possible phase I clinical trial inclusion are invited to attend the weekly treatment planning conference held every Wednesday from 9:00 a.m. to 9:30 a.m. in the Rotary House, first floor conference rooms A/B/C. Emailing the patient's name and record number to Kristie Lawhorn, RN, research nurse supervisor, by noon Tuesday is recommended, but not mandatory, to add a case to the meeting agenda.

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
Sirolimus and vorinostat	Razelle Kurzrock, MD	mTOR inhibitor combined with histone deacetylase inhibitor	Advanced cancer	Allows children any age and CNS metastases
Lapatinib and 1) sirolimus or 2) metformin	Razelle Kurzrock, MD	Tyrosine kinase inhibitor combined with mTOR inhibitor or antihyperglycemic agent	Advanced cancer	Allows children any age and CNS metastases
*KX2-391	Aung Naing, MD	Src kinase inhibitor	Advanced cancers	Allows CNS metastases
Valproic acid and 1) sorafenib 2) sunitinib 3) dasatinib 4) erlotinib 5) lapatinib or 6) lenalidomide	Aung Naing, MD	HDAC inhibitor	Solid tumors	
TAS106 and carboplatin	Aung Naing, MD	RNA polymerase inhibitor	Solid tumors	
IMC-A12 and CCI-779	Aung Naing, MD	IGF-1R and mTOR inhibitors	Advanced cancers	Allows children age 16 or older and CNS metastases
*GSK1363089	Aung Naing, MD	Met inhibitor	Solid tumors	
AZD 8055	Aung Naing, MD	mTOR inhibitor	Advanced cancers	
Bevacizumab and temsirolimus	Sarina Piha-Paul, MD	Monoclonal antibody and mTOR inhibitor	Advanced cancers	Allows children any age
IP oxaliplatin and paclitaxel plus IV paclitaxel and bevacizumab	Apostolia Tsimberidou, MD, PhD	Regional (intraperitoneal) therapy	Advanced cancers	Allows children any age and CNS metastases
Hepatic arterial infusion of cisplatin with IV Doxil	Apostolia Tsimberidou, MD, PhD	Cytotoxic, combined regional and systemic chemotherapy	Advanced Cancers	Liver predominant disease. Allows children any age and CNS metastases
Hepatic arterial infusion of paclitaxel	Apostolia Tsimberidou, MD, PhD	Cytotoxic regional therapy	Advanced cancers	Liver predominant disease. Allows children 13 or older and CNS metastases
Hepatic arterial infusion of oxaliplatin and 1) hepatic arterial infusion of fluorouracil with bevacizumab 2) systemic fluorouracil, leucovorin, bevacizumab, and cetuximab 3) bevacizumab or 4) bevacizumab and cetuximab	Apostolia Tsimberidou, MD, PhD	Regional (hepatic) chemotherapy with Avastin	Advanced cancers	Liver predominant disease. Allows children any age and CNS metastases
Hepatic arterial infusion of irinotecan and 1) bevacizumab 2) bevacizumab and oxaliplatin 3) bevacizumab and cetuximab	Apostolia Tsimberidou, MD, PhD	Regional (hepatic) and systemic chemotherapy	Advanced cancers	Liver predominant disease. Allows children any age and CNS metastases
5-azacytidine and oxaliplatin	Apostolia Tsimberidou, MD, PhD	Hypomethylating agent (azacytidine) and platinum compound (oxaliplatin)	Advanced cancers	
Hepatic arterial infusion of abraxane and IV gemcitabine and bevacizumab	Apostolia Tsimberidou, MD, PhD	Antimicrotubule agent with a nucleoside analog and anti-VEGF monoclonal antibody	Advanced cancers	Allows CNS metastases
Valproic acid and bevacizumab	Jennifer Wheeler, MD	Oral histone deacetylase inhibitor combined with monoclonal antibody against VEGF	Advanced cancers	Allows children any age
*PCI-24781	Jennifer Wheeler, MD	HDAC inhibitor	Advanced cancers	Allows CNS metastases
*MGCD265	Jennifer Wheeler, MD	VEGFR 1, 2, 3/cMET/tie/ron inhibitor	Advanced cancers	
XL147 + Taxol/carboplatin	Jennifer Wheeler, MD	PI3K inhibitor	Advanced cancers	
R4733	Jennifer Wheeler, MD	Gamma secretase	Solid tumors	
EGFR mutation (umbrella protocol)	Jennifer Wheeler, MD	Screening for EGFR mutations	Advanced cancers	
Erlotinib + cetuximab (companion to EGFR mutation umbrella protocol)	Jennifer Wheeler, MD	EGFR inhibitor and monoclonal antibody	Advanced cancers	
Erlotinib + bortezomib (companion to EGFR mutation umbrella protocol)	Jennifer Wheeler, MD	EGFR inhibitor and proteasome inhibitor	Advanced cancers	
Erlotinib + dasatinib (companion to EGFR mutation umbrella protocol)	Jennifer Wheeler, MD	EGFR inhibitor and anti-metabolite	Advanced cancers	
QBI-139	Jennifer Wheeler, MD	ribonuclease protein antagonist	Solid tumors	

* Closed to new patient entry

Upcoming PHASE I PROGRAM PROTOCOLS

Protocol	Principal Investigator	Drug Mechanisms	Diseases	Comment
MLN8237 and paclitaxel	Gerald Falchook, MD	Aurora kinase inhibitor	Solid tumors	Allows CNS metastases
EMD1204831	Gerald Falchook, MD	c-MET inhibitor	Solid tumors	Allows CNS metastases
GSK2118436 and GSK1120212	Gerald Falchook, MD	MEK and BRAF inhibitors	Solid tumors	Allows CNS metastases
Curcumin, vorinostat, and sorafenib	Siqing Fu, MD, PhD	Natural plant-derived NF- κ B inhibitor, histone deacetylase inhibitor and VEGF inhibitor	Advanced cancer	Allows CNS metastases
Azacytidine, lenalidomide, grifola frondosa scFvMEL/TNF	Siqing Fu, MD, PhD David Hong, MD	Hypomethylating agent, antiangiogenesis, and shiitake mushroom Fusion protein, monoclonal antibody	Advanced cancer Solid tumors	Allows children any age and CNS metastases Allows CNS metastases
Nab-paclitaxel, gemcitabine, bevacizumab	David Hong, MD	Recombinant monoclonal antibody, nanoparticle albumin-bound paclitaxel, chemotherapy agent	Advanced cancer	Allows children any age and CNS metastases
LY2606368	David Hong, MD	CHK1 inhibitor	Advanced cancer	
GSK1120212 and GSK2141795	Razelle Kurzrock, MD	MEK and AKT inhibitors	Solid tumor	Allows CNS metastases
VEGF121/rGEL	Razelle Kurzrock, MD	VEGF attached toxin	Advanced cancer	Allows CNS metastases
Bendamustine and bevacizumab	Apostolia Tsimberidou, MD, PhD	Cytotoxic alkylating agent, anti-VEGF monoclonal antibody	Advanced cancer	Allows CNS metastases
Lenalidomide with 1) bevacizumab 2) sorafenib 3) temsirolimus or 4) FOLFOX	Apostolia Tsimberidou, MD, PhD	Antiangiogenic agent, VEGF or tyrosine kinase or mTOR inhibitors or chemotherapy regimen	Advanced cancer	Allows CNS metastases
GSK2141795	Jennifer Wheeler, MD	AKT inhibitor	Advanced cancer	Allows CNS metastases